Proposed Decision Memo for Microvolt T-wave Alternans (CAG-00293R)

Decision Summary

CMS was asked to reconsider our current national coverage determination (NCD) on microvolt t-wave alternans (MTWA) diagnostic testing to extend coverage to the modified moving average (MMA) method. The current NCD specifically provides for coverage of MTWA using the spectral analysis method and noncovers MTWA using any other method (Section 20.30 Medicare National Coverage Determinations Manual). CMS proposes that there is insufficient evidence to conclude that the MMA method of determining MTWA is reasonable and necessary for the evaluation of Medicare beneficiaries at risk for sudden cardiac death (SCD) under section 1862(a)(1)(A) of the Social Security Act (the Act), and therefore, we propose to continue national noncoverage.

Nationally Covered Indications

Microvolt T-wave Alternans diagnostic testing is covered for the evaluation of patients at risk for SCD only when the spectral analysis method is used.

Nationally Non-Covered Indications

Microvolt T-wave Alternans diagnostic testing is non-covered for the evaluation of patients at risk for SCD if measurement is not performed employing the spectral analysis method.

We are requesting public comments on this proposed determination pursuant to section 1862(1) of the Act. We are particularly interested in comments that include new evidence we have not reviewed here or in past considerations of this NCD. After considering the public comments and any additional evidence we will make a final determination and issue a final decision memorandum.

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Proposed Decision Memo

TO: Administrative File: CAG #00293R1
Reconsideration of Microvolt t-Wave Alternans

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SUBJECT:

Proposed Decision Memorandum for reconsideration of the NCD on microvolt t-wave alternans testing.

DATE: February 14, 2008

I. Proposed Decision

CMS was asked to reconsider our current national coverage determination (NCD) on microvolt t-wave alternans (MTWA) diagnostic testing to extend coverage to the modified moving average (MMA) method. The current NCD specifically provides for coverage of MTWA using the spectral analysis method and noncovers MTWA using any other method (Section 20.30 Medicare National Coverage Determinations Manual). CMS proposes that there is insufficient evidence to conclude that the MMA method of determining MTWA is reasonable and necessary for the evaluation of Medicare beneficiaries at risk for sudden cardiac death (SCD) under section 1862(a)(1)(A) of the Social Security Act (the Act), and therefore, we propose to continue national noncoverage.

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II. Background

Cardiovascular disease is the leading cause of death in the United States. Sudden cardiac death is estimated to account for 50% of all cardiovascular deaths. There are an estimated 350,000 cases of sudden cardiac death in the U.S. yearly. Of those cases of cardiac arrest occurring outside of a hospital, being resuscitated and reaching the hospital alive, 20% survive to discharge. Ventricular tachyarrhythmic events (VTE) are responsible for 75-80% of these deaths.

MTWA testing is a non-invasive diagnostic procedure that detects minute electrical activity in a portion of the electrocardiogram (EKG) known as the t-wave. Published articles in medical journals have proposed that MTWA testing has a role in the risk stratification of patients who may be at risk for SCD from ventricular arrhythmias. Within groups of patients that may be considered candidates for implantable cardioverter defibrillator (ICD) therapy, published literature indicates that a negative MTWA test may be useful in identifying low-risk patients who are unlikely to benefit from, and who may experience worse outcomes from, ICD placement.

CMS currently covers MTWA when it is performed using the spectral analysis method. Spectral analysis is a sensitive mathematical method of measuring and comparing time and EKG signals and these are then used to calculate minute voltage changes and MTWA. Computer software then analyzes these microvolt changes and produces a report to be interpreted by a physician. The presence of significant MTWA is defined as an alternans voltage $\geq$1.9 microvolts (μV) at 0.5 cycles-per-beat with an alternans ratio $\geq$3. The absence of MTWA is defined as no evidence of alternans at 0.5 cycles-per-beat when the heart rate is sustained >105 beats/min or within 5 beats/min of maximum predicted heart rate for at least 1 min. Otherwise, MTWA is considered indeterminate. The spectral analytical method requires the patient to be stationary when obtaining the data, thus, this data cannot be acquired with ambulatory ECG monitoring such as Holter monitors.

In the MMA method of measuring t-wave alternans, electrodes placed on a patient's chest are used to obtain 24-hour ambulatory EKG recordings using a Holter monitor. These recordings are then analyzed to measure various changes in the t-wave portion of the EKG in the range of one millionth of a volt. Unlike the spectral analysis methods, the MMA method does not require that the patient reach a specific monitored heart rate nor does it require the use of specialized electrodes. Software algorithms then analyze these microvolt changes and produce a report to be interpreted by a physician.

III. History of Medicare Coverage

CMS previously reviewed scientific literature and established national coverage of MTWA diagnostic testing using the spectral analysis method. For dates of service on or after March 21, 2006, MTWA is nationally covered for the evaluation of patients at risk for SCD, only when the spectral analysis method is used.

A. Current Request

The request from GE Healthcare asks that CMS reconsider the current NCD, to grant coverage to the MMA method of measuring t-Wave Alternans.

B. Benefit Category

Medicare is a defined benefit program. An item or service must fall within a benefit category as a prerequisite to Medicare coverage §1812 (Scope of Part A); §1832 (Scope of Part B) and §1861(s) (Definition of Medical and Other Health Services) of the Act. MTWA using the MMA method is considered to be within the following benefit category: other diagnostic tests §1861(s)(3) of the Act. This may not be an exhaustive list of all applicable Medicare benefit categories for this item or service.

IV. Timeline of Recent Activities

Date	Action
August 17, 2007	CMS accepts a formal request for reconsideration of the NCD Manual Section 20.30 to include the MMA method of determining MTWA. A tracking sheet was posted on the web site and the initial 30 day public comment period commenced.
September 16, 2007	The initial 30 day public comment period ended. Thirteen comments were received.

V. FDA Status

The Food and Drug Administration (FDA) has cleared GE Medical's MTWA devices, along with various software packages used to perform MTWA testing, through the 510(k) clearance process. Clearance was obtained on December 3, 2002 (K023380) and October 30, 2003 (K032513).

VI. General Methodological Principles

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for beneficiaries. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

A detailed account of the methodological principles of study design that the agency utilizes to assess the relevant literature on a therapeutic or diagnostic item or service for specific conditions can be found in Appendix A.

Public comment sometimes cites the published clinical evidence and gives CMS useful information. Public comments that give information on unpublished evidence such as the results of individual practitioners or patients are less rigorous and therefore less useful for making a coverage determination. CMS uses the initial public comments to inform its proposed decision. CMS responds in detail to the public comments on a proposed decision when issuing the final decision memorandum.

VII. Evidence

A. Introduction

We are providing a summary of the evidence we considered during our review. The evidence reviewed to date in this decision memorandum includes the published medical literature on pertinent clinical trials of the MMA method for measuring MTWA to determine if it improves health outcomes for patients at high risk of SCD with specific consideration of patients who may receive ICDs.

B. Discussion of Evidence Reviewed

1. Question

Is the evidence adequate to conclude that MTWA testing using the MMA method improves health outcomes for Medicare beneficiaries who are candidates for ICD placement?

2. External Technology Assessments

CMS did not request an external technology assessment (TA) on this issue.

3. Internal technology assessment

The reviewed evidence was gathered from articles submitted by the requestor and a literature search of the PubMed database.

To support its request for coverage, the requestor initially submitted 11 citations. The requestor subsequently submitted 21 additional citations. These included articles on technical or methodological feasibility, unpublished articles, non-clinical study articles, articles in which the MMA method was mentioned but not reported and applications of MTWA for other than the requested indication (e.g., hypertension, cardiac pacing, mental stress). From this list, CMS excluded unpublished articles, oral presentations, editorials, review articles, studies that did not specifically address MTWA as a risk stratifier for patients eligible for ICD treatment and those lacking sufficiently detailed information on study design or discussion of results.

Literature search methods

The search terms used by CMS were:

- T-wave alternans, arrhythmia
- T-wave alternans, ventricular
- T-wave alternans, implantable cardioverter defibrillator (ICD)
- T-wave alternans, cardiac defibrillator (ICD)
- T-wave alternans, Multicenter Automatic Defibrillator Implantation Trial II (MADIT II)
- T-wave alternans, sudden cardiac death (SCD)
- T-wave alternans, ejection
- T-wave alternans, infarction
- T-wave alternans, cardiomyopathy
- T-wave alternans, primary prevention

From the PubMed search results, CMS then excluded non-English language articles, studies with fewer than 10 cases and those not involving human subjects. Using these terms and exceptions, CMS did not identify any articles in addition to those provided by the requestor.

Nieminen et al. (July 2007) studied indigenous Finnish subjects in one geographic area of Finland as a part of the Finnish Cardiovascular Study. They tested the hypothesis that t-wave alternans predicts mortality in a general population of patients referred for a clinical exercise test. According to the authors, a total of 1037 consecutive patients (673 men and 364 women) gave consent and were enrolled. The reported “mean age ± SD” [standard deviation] was 58 ± 13 years, which indicates that approximately 26-27% of the subjects were 65 years of age or older. Subjects who came for any reason for a clinically indicated exercise test at a particular Finnish university hospital between October 2001 and January 2003 and had a technically successful electrocardiogram were included in the study.

The authors inform us that the patients given the stress exercise test had one or more of the following characteristics: coronary heart disease (CHD) (46%), arrhythmia during exercise (18%), need to be evaluated for work capacity (19%), need to be checked for adequacy of CHD treatment (24%), or need for an exercise profile prior to an invasive operation (13%) or after an MI (10%). We note that authors chose to utilize the MMA method via a standard EKG instead of a Holter monitor, for reasons that are not clarified in the article.

Ninety-six percent of the stress tests were successful according to the authors. Digital EKGs were recorded and MTWA results were analyzed continuously with the time-domain MMA method. The maximum MTWA value at a heart rate (HR) of 125 beats per minute (BPM) was derived and its ability to stratify risk was tested for the following outcomes: all-cause death, cardiovascular death and SCD. There were no data on persons already having an implanted ICD or persons who had already been selected to receive an ICD.

During a follow-up period of 44 ± 7 months (mean ± SD), 59 patients died—34 due to cardiovascular causes and 25 from other causes. Of the 34, 20 were due to SCD. Multivariate analysis was performed after adjustment for age, sex, use of β-blockers, functional class, maximal HR during exercise, previous myocardial infarction, and other common coronary risk factors. The relative risk associated with a positive MTWA (65 mV cutoff) for SCD was 7.4 (95% CI, 2.8–19.4; $p < 0.001$); for cardiovascular mortality was 6.0 (95% CI, 2.8–12.8; $p < 0.001$), and for all-cause mortality was 3.3 (95% CI, 1.8–6.3; $p < 0.001$). At cutoff points of 65 mV and 46 mV, the PPV (positive predictive value - the percentage of true positives in all persons testing positive) was 8% and 3.7% respectively and the NPV (negative predictive value - the percentage of true negatives in all persons testing negative) was 98.6% and 98.7% respectively for SCD. The authors concluded that time-domain MTWA analysis powerfully predicts mortality in a general population undergoing a clinical exercise test.

Verrier et al. (2003) used a nested case-control method to analyze 15 cases and 29 controls from the large ATRAMI (Autonomic Tone and Reflexes After Myocardial Infarction, 1991-1994) study, matched for sex, age, site of MI, LVEF, thrombolysis, and beta blocker therapy. The 15 cases were selected from the 27 with cardiac arrest due to documented ventricular fibrillation or arrhythmic death. The authors report that the remaining 12 potential cases were excluded for a variety of reasons, but state that the clinical characteristics of the excluded subjects did not differ significantly from the included cases. Peak MTWA values were reported by one blinded investigator for a single 15 second period at three predetermined time intervals i.e. 15 second intervals beginning with maximum heart rate, 8:00 AM and maximum ST segment deviation, separately. They used the Wilcoxon rank sum test to compare the MMA method of measuring MTWA means between cases and controls at three predetermined time intervals. They *a priori* defined high MTWA as being > the 75^{th} percentile among the controls.

The authors report that MTWA magnitude was similar at baseline in cases and controls, but that mean MTWA in microvolts was significantly higher in cases than controls at maximum heart rate and at 8:00 AM in lead V_5. There was a similar but nonsignificant trend in V_1. The mean maximum MTWA during maximum ST segment deviation was similar in cases and controls in both leads. Odds ratios for cardiac arrest or sudden death due to arrhythmia were increased for cases versus controls at maximum heart rate and at 8:00 AM.

Cox et al. (2006) studied MTWA simultaneously using spectral analysis and the MMA method during pacing (< 110 beats/min) in 41 patients. The authors stated that the 41 patients had no prior sustained ventricular arrhythmias, and were referred for risk stratification. Patients were age 67 ± 9 years and 85% had coronary disease. Thirty nine of 41 patients were male. They measured MTWA during ventricular (ventricular + atrial) pacing, although comparisons with 'traditional' atrial pacing again found concordance. Over 542 ± 311 days follow-up, there were 11 deaths or sustained ventricular arrhythmias ('events').

Positive spectral analysis MTWA (1.9 μV) predicted patients with ventricular arrhythmia events from those without events (p= 0.02). Receiver-operating characteristics for the MMA method of measuring MTWA showed that the cutpoint of 10.75 μV was optimal for the combined endpoint. Kaplan-Meier analysis using this cutpoint trended to predict events (p = 0.06), while the MMA method of measuring MTWA combined with spectral analysis MTWA predicted events (p = 0.01) the authors stated. This study is small and limited to males (=95%). It employed a composite clinical endpoint instead of the endpoint of sustained arrhythmias or sudden cardiac arrest. The MMA method of MTWA measurement is usually tested at a HR of 125 beats/min and in this study it was tested at 110.

We also note that new evidence casts doubt on the usefulness of MTWA testing. The MASTER 1 trial is designed to evaluate MTWA testing for risk stratification for life threatening VTEs among post-MI patients with impaired ejection fraction undergoing ICD implantation. (See: Clinicaltrials.gov Identifier NCT00305240.) In a presentation by Dr. Theodore Chow at the American Heart Association Annual Scientific Session, Orlando, Florida, November 2007, the following abstract was reported.

> Among post-MI patients with impaired EF undergoing ICD implantation, risk stratification using MTWA was not associated with difference in prediction of life-threatening ventricular tachyarrhythmic events.

Additionally,

> Non-negative MTWA associated with higher risk of death, but not specifically arrhythmic death, suggesting positive MTWA test may just identify cohort of sicker patients, as evidenced by increase in baseline risk.

The full report of MASTER 1 has not been published as we write this proposed decision memorandum. We anticipate reviewing these data more fully for the final decision memorandum.

4. MedCAC

A Medicare Evidence Development and Coverage Advisory Committee (MedCAC) meeting was not convened on this issue.

5. Evidence-based guidelines

No evidence-based guidelines are available for the use MTWA using the MMA method for patients who are candidates for ICD placement.

6. Professional Society Position Statements

The Heart Rhythm Society submitted a letter that did not support coverage of MTWA using the MMA method for the requested indications. No references were cited in this letter.

7. Expert Opinion

We did not receive any expert opinions on the use of MTWA using the MMA method.

8. Public Comments

Initial Comment Period: August 17, 2007 – September 17, 2007

Timely public comments are summarized below:

CMS received a total of thirteen comments during the first public comment period. Ten out of the thirteen comments stated that there was insufficient evidence to expand coverage to the MMA method. Two of these ten individuals cited specific research studies within their comments. Of the remaining three commenters, one felt that MTWA should be required prior to ICD placement but did not address the question as it relates to the MMA method versus spectral analysis. One commenter was in favor of coverage but indicated that randomized trials are needed to determine if either method can guide ICD therapy. The last commenter indicated that the MMA method was effective for risk stratification and should be covered nationally; however, this commenter is from the same organization as the entity that requested the reconsideration.

VIII. CMS Analysis

National coverage determinations (NCDs) are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally under §1869(f)(1)(B) of the Act. In order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Moreover, with limited exceptions the expenses incurred for items or services must be “reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.” See §1862(a)(1)(A)of the Act. This section presents the agency’s evaluation of the evidence considered and conclusions reached for the assessment

As a diagnostic test, MTWA would not be expected to directly change health outcomes. Rather, a diagnostic test affects health outcomes through changes in disease management brought about by physician actions taken in response to test results. Such actions may include decisions to treat or withhold treatment, to choose one treatment modality over another, or to choose a different dose or duration of the same treatment. 42 CFR 410.32(a) states in part, “…diagnostic tests must be ordered by the physician who is treating the beneficiary, that is, the physician who furnishes a consultation or treats a beneficiary for a specific medical problem and who uses the results in the management of the beneficiary’s specific medical problem.”

Question

Is the evidence adequate to conclude that MTWA testing using the MMA method improves health outcomes for Medicare beneficiaries who are candidates for ICD placement?

Analysis

Extensive clinical research has revealed that patients with symptoms of or at risk for life threatening arrhythmias who also test positive for T-wave alternans have a higher risk for subsequent development of sudden cardiac events including sudden death. Those who test negative have a lower risk. However, many patients have indeterminate results. MTWA using a spectral analysis algorithm as a stratification tool may help to identify individual patients from high risk populations (e.g., those with ischemic and nonischemic cardiomyopathy, dilated cardiomyopathy, post myocardial infarction, MADIT II-type, or SCD-HeFT-type) who are actually at low-risk for SCD and who thus may be able to avoid ICD placement. CMS has previously determined that it is possible to classify those patients who test positive or indeterminate for MTWA (i.e., those more likely to benefit from ICD implantation), and those who test negative for MTWA (i.e., those less likely to benefit from ICD implantation). This determination was made based on the evidence available at that time for the spectral analysis method.

The question before us could be addressed either by independent demonstration of a clinical benefit of the MMA method of measuring MTWA or by demonstration of substantial comparability of the MMA and SA methods of measuring MTWA. The evidence we reviewed focused on the former.

The relevant evidence base for the MMA method algorithm is comparatively sparse. We are concerned that the narrow subject populations in the trials limit the generalizability of study results to Medicare beneficiaries. Other limitations of this body of literature include small sample sizes (Lampert, Shusterman, Burg et. al. 2005; Verrier, Nearing, La Rovere et al. 2003, Kop et al 2004), the use of simulations or non-clinical outcome measures (Nearing, Huang, Verrier, 2002, Nearing, Verrier, 2001, Martinez, Olmos, 2005; Shusterman, Goldberg, London, 2004,), and the lack of control groups (Lampert, Shusterman, Burg et al. 2005). Other studies had MTWA measured for non-cardiac indications such as mental stress (Kop et al 2004, Lampert, Shusterman, Burg et al. 2005) The 2005 article by Verrier et al. is an expert opinion, so we did not review it.

Results of the 2003 study by Verrier et al. suggest that the clinical diagnostic information provided by the MMA method is comparable in some respects to that provided by spectral analysis. Though the ATRAMI study from which the study data were later drawn was prospective and included 1284 post-myocardial infarction patients, the Verrier study only examined 15 cases and 29 controls, using data that was originally collected for a purpose other than MTWA testing. The limitations of small sample size and limited study design along with very large and thus imprecise confidence intervals lead us to assign lesser weight to its conclusions.

The Nieminen study has a much larger sample size, with 1037 participants. A strength of the study are that approximately 26% of its subjects were 65 years or older and therefore of Medicare age. Without explanation, the authors chose to apply the MMA method to a standard EKG instead of a Holter monitor. We are not aware of any advantages or disadvantages of such application, and we invite public comment on this point. Many participants (over 1000) underwent exercise stress tests; the test had good negative predictive value for certain MMA method cutoff points. The reported follow-up time of 44 ± 7 months is of sufficient duration.

We will describe in detail our reservations about the Nieminen study because this is the only substantial clinical trial existing or published on the MMA method.

1) The paper does not report the baseline status of the subjects (coronary heart disease, arrhythmia during exercise, need to be evaluated for work capacity, or need for an exercise profile prior to an invasive operation or after an MI) relative to which ones eventually had SCD or other heart related death. Since these factors are potential confounders, the lack of separate consideration for each one is problematic and clouds the results.

2) The ethnicity of the study population apparently differs sufficiently from the Medicare beneficiary population to limit the generalizability of its conclusions. Though the racial makeup is not mentioned, CMS does not have evidence that Hispanic and African American populations are proportionately represented in this study since over 98% of the population of Finland is of Finnish (93 + %) or Swedish ethnicity.

3) The EF was only determined for approximately 50% of the study population, and we are uncertain as to whom that applies to (i.e., which half of the subjects by baseline status). This confounds the analysis.

4) The study does not compare the MMA method of measuring MTWA to spectral analysis MTWA. While this is not a requirement, i.e. the requestor can attempt to demonstrate a clinical benefit of the MMA method of measuring MTWA on its own merits; it does limit the potential relevance of evidence regarding spectral analysis to the current question. A comparison might be helpful since the evidence of benefit for the MMA method itself is limited.

5) Cutoff points were determined after the fact rather than prospectively. As in other articles describing critical values for prediction of SCD via the MMA method, there is neither a standard lead nor a standard mV cutoff point.

6) This study was performed in a more general population undergoing routine exercise testing whereas CMS is interested in populations at higher risk for ventricular arrhythmia events or SCD event and evaluation for ICD implantation. Therefore, these data have limited generalizability to the Medicare population having the prerequisites for MTWA testing.

7) According to the study protocol published in 2006 (Nieminen et al BMC Cardiovascular Disorders 2006),

The participant pool consists of patients who undergo exercise stress tests at Tampere University Hospital. All the consecutive patients coming in for an exercise stress test and willing to participate in the study have been and will be recruited between October 2001 and December 2007. Our goal is to recruit roughly 5,000 patients. Currently, the research group is actively analyzing the data on the 2,212 patients (1,400 men and 812 women) recruited by the end of 2004.

CMS was unclear about the apparent discrepancy between the 1037 subjects in the 2007 MTWA study under discussion and the availability of much more data at the time the study was published. Are the data on all those patients after the first 1037? Did they change techniques in January 2003, or was there some other change? We also question why the protocol was published in 2006 since the study was to be ongoing from 2001 forward. The protocol for this study does mention t-wave alternans as a goal of measurement to see if it is linked with mortality.

8) The report does not say it was prospectively planned from the outset in 2001; i.e. it appears to have been an afterthought. It has no control group, which is a significant methodologic weakness.

9) We are also not told what percent of patients were not willing to participate and how their demographic characteristics compare to those of the 1037 who gave consent; indicating possible mishandling of indeterminate findings and skewing of results.

10) The study reports that 96.6% of 1037 patients had technically successful exercise tests. They did not report why the other 3.4% were unsuccessful and if they had characteristics that would have changed the outcome since there were approximately 35 of them. That is, they may have all not completed the stress test successfully for some reason (health or otherwise) and that would affect the results.

11) This is not a randomized control trial but a consecutive series.

After careful examination CMS finds that the evidence base supporting the MMA method of measuring MTWA is limited, and though suggestive of benefit, is not yet convincing. We find that the evidence is not sufficient for CMS to determine that MTWA via the MMA method is reasonable and necessary for the identification of Medicare beneficiaries at risk of SCD who would benefit from ICD placement.

CMS anticipates reviewing the full published MASTER 1 report prior to issuing a final decision memorandum. We agree with the commenter who noted the need for additional trials about this technology, and we believe that this trial and other ongoing trials will be important additions to the evidence base. We are requesting public comment on the reported findings of the MASTER 1 trial, specifically with regard to whether CMS should continue to cover MTWA in general, regardless of the method used.

IX. Proposed Conclusion

CMS was asked to reconsider our current national coverage determination (NCD) on microvolt t-wave alternans (MTWA) diagnostic testing to extend coverage to the modified moving average (the MMA) method. The current NCD specifically provides for coverage of MTWA using the spectral analysis method and noncovers MTWA using any other method. CMS proposes that there is insufficient evidence to conclude that the MMA method of determining MTWA is reasonable and necessary for the evaluation of Medicare beneficiaries at risk for sudden cardiac death (SCD) under section 1862(a)(1)(A) of the Social Security Act, and therefore, we propose to continue national noncoverage.

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Bibliography

Bhargava V, Watanabe K, Froelicher VF. Progress in computer analysis of the exercise electrocardiogram. American Journal of Cardiology 1981;47:1143-1151.

Bigi R, et al. Exercise versus recovery electrocardiography in predicting mortality in patients with uncomplicated myocardial infarction. European Heart Journal 2004;25:558-564.

Bloomfield DM, Hohnloser SH, Cohen RJ. Interpretation and classification of microvolt T wave alternans tests. Journal of Cardiovascular Electrophysiology 2002;13(5):502-512.

Cox V, Patel M, Kim J, Liu T, Sivaraman G, Narayan SM. Predicting arrhythmia-free survival using spectral and modified-moving average analyses of T-wave alternans. PACE 2007;30:352-358.

Exner DV et al. Noninvasive assessment of sudden death risk after myocardial infarction—results of the REFINE study. Heart Rhythm 2007;4(5):S94.

Exner DV. CMS public comment for microvolt T-wave alternans (CAG-00293R), 9/5/07.

Exner DV, Kavanagh KM, Slawnych MP, Mitchell LB, Ramadan D, Aggarwal SG, Noullett C, Van Schaik A, Mitchell RT, Shibata MA, Gulamhussein S, McMeekin J, Tymchak W, Schnell G, Gillis AM, Sheldon RS, Fick GH, Duff HJ for the REFINE Investigators. Noninvasive risk assessment early after a myocardial infarction. The risk estimation following infarction, noninvasive evaluation (REFINE) Study. Journal of American College of Cardiology, in press.

Gehi AK, Stein RH, Metz LD, Gomes JA. Microvolt T-wave alternans for the risk stratification of ventricular tachyarrhythmic events: A meta-analysis. Journal of American College of Cardiology 2005;46:75– 82.

Hostetler B, Xue J, Young B, Kaiser K, Findeis M, Gutterman D. Detect short run of TWA event with time-domain algorithm. Computers in Cardiology 2005;32:483–486.

Huikuri HV, Castellanos A, Myerburg RJ. Sudden death due to cardiac arrhythmias. New England Journal of Medicine 2001;345:1473–82.

Kaiser W, Findeis M. Artifact processing during exercise testing. Journal of Electrocardioly 1999;32 Suppl:212-219.

Kaiser W. Findeis M. Novel signal processing methods for exercise ECG. International Society for Bioelectromagnetism 2000;2:60-65.

Kaiser W, Findeis M, Young B. Improving T-wave alternans measurement quality by reducing noise and artifact. Computers in Cardiology 2004;31:445-448.

Kaufman ES, Bloomfield DM, Steinman RC, Namerow PB, Costantini O, Cohen RJ, Bigger JT. “Indeterminate” microvolt T-wave alternans tests predict high risk of death or sustained ventricular arrhythmias in patients with left ventricular dysfunction. Journal of American College and Cardiology 2006;48:1399–1404.

Klingenheben T, Gronefeld G, Li Y-G, Hohnloser SH. Effect of metoprolol and d,l-sotalol on microvolt-level T-wave alternans: results of a prospective, double-blind, randomized study. Journal of American College Cardiology 2001;38:2013–9.

Klingenheben T, Ptaszynski P, Hohnloser SH. Quantitative assessment of microvolt T-wave alternans in patients with congestive heart failure. Journal of Cardiovascular Electrophysiology 2005;16(6):620-4.

Kop WJ, Krantz DS, Nearing BD, et al. Effects of acute mental stress and exercise on t-wave althernans in patients with implantable cardioverter defibrillators and controls. Circulation 2004;109:1-6.

Lampert R, Shusterman V, Burg MW, et al. Effects of psychologic stress on repolarization and relationship to autonomic and hemodynamic factors. Journal of Cardiovascular Electrophysiology 2005;16:372-377.

Lauer MS, et al. Exercise-induced QT/R-R-interval hysteresis as a predictor of myocardial ischemia. Journal of Electrocardiology 2006;39:315-323.

Martinez JP, Olmos S. Methodological principles of T wave alternans analysis: a unified framework. IEEE Transactions on Biomedical Engineering (2005 Apr) 52(4):599-613.

Meyer CR, Keiser HN. Electrocardiogram baseline noise estimation and removal using cubic splines and state-space computation techniques. Comput Biomed Res 1977;10:459-470.

Mickelson JK, Veterans Affairs ACME Investigators, et al. Is computer interpretation of the exercise electrocardiogram a reasonable surrogate for visual reading?. Clinical Cardiology 1997;20:391-397.

Narayan SM. T-wave alternans and susceptibility to ventricular arrhythmias. Journal of American College of Cardiology 2006;47:269-281.

Nearing BD, Verrier RL. Modified moving average method for T-wave alternans analysis with high accuracy to predict ventricular fibrillation. Journal of Applied Physiology 2002a;92:541-549.

Nearing BD, Verrier RL. Progressive increases in complexity of T-wave oscillations herald ischemia-induced VF. Circ Res 2002b;91:727-732.

Nearing BD, Verrier RL. Tracking heightened cardiac electrical instability by computing interlead heterogeneity of T-wave morphology. Journal of Applied Physiology 2003;95:2265-2272.

Nieminen T, Lehtimäki T, Viik J, Lehtinen R, Nikus K, Kööbi T, Niemelä K, Turjanmaa V, Kaiser W, Huhtala H, Verrier RL, Huikuri H, Kähönen M. T-wave alternans predicts mortality in a population undergoing a clinically indicated exercise test. European Heart Journal, published on line July 25, 2007.

Shusterman V, Goldberg A, London B. Upsurge in T-wave alternans and nonalternating repolarization instability precedes spontaneous initiation of ventricular tachyarrhythmias in humans. Circulation 2006;113:2880-2887.

Simoons ML et al. Quantitation of exercise electrocardiography. Circulation 1981;63:471-475.

Verrier RL, Nearing BD, LaRovere MT, Pinna GD, Mittleman MA, Bigger JT, Schwartz PJ for the ATRAMI Investigators. Ambulatory ECG-based tracking of T-wave alternans in post-myocardial infarction patients to assess risk of cardiac arrest or arrhythmic death. Journal of Cardiovascular Electrophysiology 2003;14:705-711.

Verrier RL, Kwaku KF, Nearing BD, Josephson ME. T-wave alternans: Does size matter? [Invited editorial on Klingenheben et al 2005]. Journal of Cardiovascular Electrophysiology 2005;16:225-228.

Xue J. Rowlandson GI. Effect of noise on frequency and time domain methods of T-wave alternans. Computers in Cardiology 2004:449-452.

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